# EFFECT OF HIGH ALTITUDE ON BLOOD COUNTS.

A. MANSFIELD HOLMES, A. M., M. D., DENVER, COLO.

Much speculation has resulted from the various investigations on the influence of altitude on blood counts. This subject involves so many factors that if the results are to be of scientific value much care must be taken both in the accuracy of the technique employed, and in the interpretation of the phenomena. My studies in hematology have, for some time, directed my attention to this problem. Many interesting studies have been made in this line of work in the Alps and other parts of the world; but so far as I have been able to ascertain, a careful study of this subject has not been made in the mountains of the United States. The altitude of Pike's Peak, in the vicinity of Denver, has presented the opportunity for making such a study. I, however, was not able to avail myself of this opportunity until the early part of last September (1898).

All hematologists recognize the fact that the counting of the red and white cells of the blood is a more or less inexact procedure. Discrepancies are unavoidable; but for scientific purposes precautions can be taken which diminish these errors to the minimum. Similar difficulties are met with in the estimation of the hemaglobin, an approximately accurate estimate of which requires extended practice and a keen sense of color perception. A few words as to the method adopted in this study are probably not out of place. The instruments employed were a microscope, Fleischel's hemometer, and Thoma-Zeiss hemacytometer. It might be as well to state at this time that a uniform method of study was used in each count, the same instruments were employed, and the usual sources of error in making such counts were, as far as possible, avoided.

In normal blood it has been ascertained that for every white cell there are about five hundred red cells. It is evident to all who have used the Thoma-Zeiss instrument that in making a count of the red and white cells over an area large enough to furnish five hundred red cells, there may be no white cell found, while in an adjacent area two or more white cells may be found. Therefore, the ratio of red cells to white cells, as determined by a count of one such area, may have a wide variation. Mathematically, if we let X equal the number of white cells, then $\frac{500}{X}=R=$ *ratio of red to white cells.* When $X=0$, $R=\infty$ (infinity); $X=1$, $R=500$; $X=2$, $R=250$; etc. On the average, when X is equal to 1, we may conclude that the probability of error in the count of white and red cells is 500 against the white. How may we diminish the probability of error? This is a question which I have considered, and for my own use have adopted the following method:

I use the highest power dry lens that can be focussed on the blood in the Thoma-Zeiss cell. By counting the red cells in fifty squares, and the white cells in four hundred squares we reduce the *ratio of error* eight times; $500 \div 8 = 62,\ 5 = R'$. Also I use an objective which will give a field of vision with a diameter five or six times greater than the side of one of the squares of the Thoma-Zeiss cell. Any variation in either direction can be readily adjusted by increasing or decreasing the tube length of the microscope. Using my Bausch and Lomb microscope with a No. 6 lens, 1 inch objective, and tube length 163 mm., I obtain a field of vision with a diameter equal to the side of six squares, which equals $\frac{6}{20}$ mm. Therefore $r^2=\frac{9}{400}$; the area, $\pi r^2=3.1416 \times \frac{9}{400}=.070686$ sq. mm., = area of field of view. In other words, by counting 14.14 fields of view we obtain the number of blood cells in 1 sq. mm. By counting 84.84 fields of view we obtain the count of cells equal to 6 sq. mm. Therefore by adding the number of white cells found in the 400 squares to those found in 84.84 fields of view beyond the checkered scale, we obtain the number of white cells found in 7 sq. mm. of surface, which is the equivalent of 99 fields of view. (84.84 plus 14.14=98.98). The

total number divided by 7, the number of sq. mm., will give an average very close to the true number. The probable error is now reduced from 62.5 to 8.9=(62.5÷7=8.9=R″).

In the following studies I uniformly counted the red cells in fifty squares of the Thoma-Zeiss cell, or the equivalent of one-eighth of one sq. mm. of surface. The white cells were counted over a surface equivalent to 7 sq. mm. The blood was diluted with Toison's Solution, 1 to 100; thoroughly mixed, and studied immediately. Two counts were made, each coming from the same diluted specimen of blood, the mixture being thoroughly agitated before taking the drop utilized for counting. The shortest possible time intervened between the two counts; the same Thoma-Zeiss instrument was used, and the same precautions used in mixing the contents of the instrument before the drops were taken. In each count, as far as possible, a drop of the same size was used and the same care exercised in applying the cover glasses. The blood studied was taken from the tip of the finger, punctured by a triangular pointed needle. In each study I have adopted the average of the two counts for my report as being approximately closer to the actual number.

I have been particularly interested in comparing the results of the first and second counts made from the same diluted specimen of blood, and have also compared these estimates with those obtained by the use of Deland's hematocrit.

In my experience the Thoma-Zeiss instrument has been more satisfactory, although I must confess that I have not used the hematocrit except on a few occasions, and then for the purpose of comparing the two instruments. In the following study I made use of my own blood. In this connection it will be necessary to be, to a slight degree, personal. At the time of making the study I was in good health. I was, however, in need of rest. I left Denver on September 8th, 1898, for Colorado Springs, and commenced the experiments on the following day.

First Study.—Made at Dr. Gildea's residence, Colorado Springs, September 8th, 1898, at 11:45 a. m., two hours after

breakfast. The temperature was 52° F. The count resulted as follows: White cells, 10,700; red cells, 4,968,000 per c. mm. Hemaglobin unfortunately was not estimated at this time on account of not having the instrument at hand.

It was my intention to ascend Pike's Peak on the following day, but a storm prevented. On the second day following I made the ascent with the following report:

SECOND STUDY.—Made at the Iron Springs Hotel, Manitou, Colorado, September 11th, 1898, 6:30 a. m., before breakfast. Temperature, 45° F. The count was as follows: White cells, 8,900; red cells, 5,104,000 per c. mm. Hg. 100 per cent.

Immediately after completing this count I breakfasted and took the train for Pike's Peak, arriving at the top of the Peak at 11 a. m. Through the courtesy of Mr. B. M. Rastall, the agent of the Pike's Peak railroad at the top of the mountain, I was permitted to use one of the windows of the station, the building formerly used as the United States Signal Station.

THIRD STUDY.—Made on top of Pike's Peak, 11:15 a. m. Temperature 15° F. Storming. Blood taken before luncheon. Count: White cells, 8,000; red cells, 5,668,000 per c. mm. Hg. 95 per cent.

FOURTH STUDY.—Made on top of Pike's Peak, 2:15 p. m., three hours later. Temperature 9° F. Storming. Blood taken immediately after luncheon. Count: White cells, 9,300; red cells, 5,840,000 per c. mm.

On completing this study the train was ready to return to Manitou and I was unable to estimate the hemaglobin.

FIFTH STUDY.—Made at the Iron Springs Hotel, Manitou, 9 p. m. on the same day. Temperature 40° F. Moderating. Blood taken two hours after dinner. Count: White cells, 10,800; red cells, 5,352,000 per c. mm. Hg. 100 per cent.

For convenience I have arranged the data of the foregoing studies in tabulated form.

TABLE I.—STUDIES OF MY OWN BLOOD.

| | Time | Place | Altitude | Leucocytes per c. mm. | Red Cells per c. mm. | Hg. per c. | Temp. |
|---|---|---|---|---|---|---|---|
| First Study | Sep. 9, '98 11.18 a. m. | Dr. Gildea's office, Colo. Springs, Colo. | 6,098* | 10,700 | 4,968,000 | | 52° F. |
| Second Study | Sep. 11, '98 6.30 a. m. | Iron Springs Hotel, Manitou, Colo. | 6,318 | 8,960 | 5,104,000 | 100 | 45° F. |
| Third Study | Sep. 11, '98 11.15 a. m. | Top of Pike's Peak | 14,134 | 8,000 | 5,668,000 | 95 | 15° F. Storming |
| Fourth Study | Sep. 11, '98 2.15 p. m. | Top of Pike's Peak | 14,134 | 9,300 | 5,840,000 | | 9° F. Storming |
| Fifth Study | Sep. 11, '98 9.00 p. m. | Iron Springs Hotel, Manitou, Colo. | 6,318 | 10,800 | 5,352,000 | 100 | 40° F. Moderating |

*The altitudes in this table are those obtained from the U. S. Signal Service.

During the short period that I remained at the top of the mountain, I ascertained that Mr. Rastall, the agent of the railroad, had been residing there for almost six months, and had made only occasional trips to Manitou, and on these trips never remained longer than a few hours. Through the courtesy of Mr. Rastall I was permitted to study his blood during the time I was at the top of the mountain, and he kindly returned to Manitou with me to enable me to make a second study, to observe the effect of a sudden change to a lower altitude.

First Study.—Made on top of Pike's Peak, September 11, 1898, 1 p. m. Temperature 9° F. Storming. Blood taken immediately after luncheon. Count: White cells, 10,600; red cells, 6,788,000 per c. mm. Hg. 110 per cent.

Second Study.—Made at Iron Springs Hotel, September 11, 1895, 3:30 p. m. Temperature 40° F. Modeating. Blood taken before dinner. Count: White cells, 15,500; red cells, 6,620,000. Hg. 110 per cent.

These observations are recorded in tabular form on the opposite page (Table II).

Blood films were also taken at the time of making the various counts. These films have been stained and a differential count made. The tabulated report of these differential counts both from my own blood (Table III) and from Mr. Rastall's (Table IV), are given on page 184.

TABLE II.—STUDIES OF MR. RASTALL'S BLOOD.

| | Time | Place | Altitude | Leucocytes per c. mm. | Red Cells per c. mm. | Hg. per c. | Temperature |
|---|---|---|---|---|---|---|---|
| First Study | Sep. 11, '98 1.00 p. m. | Top of Pike's Peak | 14,134 | 10,600 | 6,788,000 | 110 | 9° F. Storming |
| Second Study | Sep. 11, '98 5,30 p. m. | Iron Springs Hotel, Manitou, Colo. | 6,318 | 15,500 | 6,620,000 | 110 | 40° F. Moderating |

TABLE III.—DIFFERENTIAL COUNTS OF MY OWN BLOOD.

| | Time | Place | Altitude | S. L. | L. L. | Trans. | Phag. | Eos. |
|---|---|---|---|---|---|---|---|---|
| First Study | Sep. 11, '98 6.30 a. m. | Iron Springs Hotel, Manitou | 6,318 | 34 | 11 | 1 | 54 | 0 |
| Second Study | Sep. 11, '98 11.15 a. m. | Top of Pike's Peak | 14,134 | 30 | 8 | 1 | 60 | 1 |
| Third Study | Sep. 11, '98 2.15 p. m. | Top of Pike's Peak | 14,134 | 25 | 10 | 1 | 63 | 1 |
| Fourth Study | Sep. 11, '98 9.00 p. m. | Iron Springs Hotel, Manitou | 6,318 | 19 | 18 | 0 | 63 | 0 |

TABLE IV.—DIFFERENTIAL COUNTS OF MR. RASTALL'S BLOOD.

| | Time | Place | Altitude | S. L. | L. L. | Trans. | Phag. | Eos. |
|---|---|---|---|---|---|---|---|---|
| First Study | Sep. 11, '98 1.00 p. m. | Top of Pike's Peak | 14,134 | 39 | 4 | 1 | 53 | 3 |
| Second Study | Sep. 11, '98 5.30 p. m. | Iron Springs Hotel, Manitou | 6,318 | 30 | 7 | 0 | 61 | 2 |

Let us now compare the foregoing studies and observe the effects produced on the blood count by the sudden changes in altitude. By referring to Table I, it will be observed: First, that between the second and third studies there was an interval of four hours and forty-five minutes. Second, during this period I made the ascent from the Iron Springs Hotel, Manitou, to the old Signal Station at the top of the Peak; the increase in altitude being 7,816 feet, or, approximately, one mile and a half. Third, during this period the red cells showed an increase of 564,000 for each c. mm. Fourth, these two counts were made before breakfast and luncheon, respectively, and yet the variation in the count of white cells was scarcely apparent. Fifth, during the interval of three hours between the third and fourth studies, while remaining on the top of the mountain, the number of red cells made a further increase of 172,000. In other words, during a period of seven hours and forty-five minutes the number of red cells increased 736,000 per each c. mm. Sixth, in the fifth study, made on returning to Manitou, equally as important phonomenon was observed. The interval between the fourth and fifth studies was six hours and forty-five minutes. During this period there was a decrease in altitude of 7,816 feet, and the number of red cells decreased 488,000 per each c. mm.

It will therefore be recognized from these studies: First, that a sudden change from a low to a high altitude produces *a rapid increase* in the number of red cells. Second, that a sudden change from a high to a low altitude produces *a rapid decrease* in the number of red cells.

The percentage estimation from Table I is as follows: Taking the count made at Manitou in the morning as the standard, the first count made on top of the mountain, four hours and forty-five minutes later, shows an increase of 11.5 per cent. The second count made on top of the mountain, three hours later, shows an increase of 14.42 per cent. Hence there was an increase of 2.92 per cent during the three hours on the top of the mountain.

On returning to Manitou in the evening the count remained 4.86 per cent higher than in the morning before starting for the top of the mountain. It will therefore be observed:

First. That the red cells increase *immediately* on making the ascent of the mountain.

Second. That the number continues to increase during a residence on the mountain.

Third. That the number suddenly diminishes on returning to a lower altitude.

Fourth. That the rate of decrease is not as pronounced as the rate of increase.

By comparing the second study of Mr. Rastall's blood, made at the Iron Springs Hotel, Manitou, with the first study, made at the top of the mountain four hours and thirty minutes earlier, we observe a decrease of 168,000 per each c. mm., or 2.47 per cent. By making a similar comparison of my own studies, comparing the fifth study with the fourth, we observe a decrease of 8.35 per cent, the interval between the studies being six hours and forty-five minutes. If these two cases are to be compared, it would seem that the blood of persons residing in a high altitude for a long period is affected to a less degree on returning to a lower altitude, than that of one who remains in a high altitude for a short time.

Numerous explanations have been offered to account for the apparent increase in the number of red cells in high altitudes; but before proceeding to look for an explanation, the factors which may, directly or indirectly, influence this change, should be considered. In order to eliminate, as far as possible, all factors except those due directly to altitude, the shortest possible intervals between the counts should be considered of not a little importance. The long intervals between such counts in the majority of the reports made heretofore, impressed me with the necessity of making counts with short intervals between them, and yet to have the advantage of the great difference in altitude. Pike's Peak, with its great elevation and a railroad running to the top, offers advantages for such a study not equalled at any other point.

The U. S. Signal Station was opened at the top of Pike's Peak September 8, 1892, and remained until October 1, 1894. The records of this Bureau show that for September, 1893, and September, 1894, the mean atmospheric pressure was equivalent to 17.91 cubic inches of mercury. Also the mean temperature for September, 1893, was 32.4° F., and for September, 1894, 29.2° F. It is estimated that one cubic inch of mercury at 4° C. weighs .49 pound avoirdupois. Hence, the weight of 17.91 cubic inches of mercury will be nearly 8.79 pounds. Therefore, the mean atmospheric pressure on Pike's Peak during September, 1893 and 1894, was approximately 8.79 pounds to the square inch.

Denver is one mile above sea-level. The atmospheric pressure at such an elevation is about twelve pounds to the square inch. This is about three pounds to the square inch less than at sea-level. A person passing suddenly from sea-level to such an altitude frequently experiences a sudden dilation of his entire vascular system as a result of the diminished resistance of the atmospheric pressure. After a prolonged residence at such an elevation, the nervous system adjusts itself to the changed conditions and very little inconvenience is experienced. Those who have made the trip to the top of Pike's Peak have experienced the effects of the diminishing atmospheric pressure from 12 pounds to 8.79 pounds.

The smaller amount of oxygen in the atmosphere at high altitudes is also an important factor. Red cells possess a strong affinity for oxygen, and are distinctly oxygen carriers.

Each organism is accustomed to, and demands, a definite amount of oxygen. The respiration and circulation are automatically adjusted in accordance with the ease or difficulty with which this need is satisfied.

Under the conditions existing in high altitudes the difficulty of supplying the organism with the needed oxygen is increased. Hence, it would seem that under such conditions there is a need for a greater activity of the total volume of red cells, to absorb the amount of oxygen necessary for the organism. This necessarily brings into activity many red cells which, under

different conditions, probably remain in a more or less quiescent state in deeper portions of the body.

How far these influences are responsible for the variation in the count of the red cells of the blood at varying altitudes, it is not the purpose of this study to investigate. The able experiments of Regnard, Egger and others have gone extensively into this department of the study.